

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. REGISTRATION NO.

22-R-0139

CUSTOMER NO.

35171

FORM APPROVED
OMB NO. 0579-0036

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

2. HEADQUARTERS RESEARCH FACILITY (Name and Address, as registered with USDA, include Zip Code)

SANOI AVENTIS
1041 ROUTE 202-206, MAILSTOP BRW JR2-203 A
BRIDGEWATER, NJ 08807
(908) 231-2334

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets if necessary.)

FACILITY LOCATIONS(sites)

(b)(2)High, (b)(7)f

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28 February - 30 Sep 2006

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY (Attach additional sheets if necessary or use APHIS FORM 7023A)

A. Animals Covered By The Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes.	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain- relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used.	E. Number of animals upon which teaching, experiments, research, surgery or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. (An explanation of the procedures producing pain or distress in these animals and the reasons such drugs were not used must be attached to this report)	F. TOTAL NO. OF ANIMALS (Cols. C + D + E)
4. Dogs	54	110	1	4	169
5. Cats	0	0	0	0	0
6. Guinea Pigs	15	1582	1564	33	3194
7. Hamsters	0	21	0	0	21
8. Rabbits	0	98	130	0	228
9. Non-Human Primates	14	4	45	0	63
10. Sheep	0	0	0	0	0
11. Pigs	0	0	0	0	0
12. Other Farm Animals	0	0	0	0	0
13. Other Animals	0	0	0	0	0

ASSURANCE STATEMENTS

- 1) Professionally acceptable standards governing the care, treatment, and use of animals, including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during, and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility.
- 2) Each principal investigator has considered alternatives to painful procedures.
- 3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). A summary of all the exceptions is attached to this annual report. In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.
- 4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL

(Chief Executive Officer or Legally Responsible Institutional official)

I certify that the above is true, correct, and complete (7 U.S.C. Section 2143)

b6, b7c

DATE SIGNED

11/17/06

November 14, 2006

USDA Annual Report

Registration #: 22-R-0139 (29 Feb 2006 – 30 Sep 2006)

Explanation of Category 'E' Animals

1. Number of Animals and Species Used in:

b4

Used: 308 Guinea Pigs
Number of Category E animals: 2

b4

Used: 10 Guinea Pigs
Number of Category E animals: 2

b4

Used: 104 Dogs
Number of Category E animals: 3

b4

Used: 12 Dogs
Number of Category E animals: 1

b4

Used: 2322 Guinea pigs
Number of Category E animals: 29

2. Procedure Used:

b4

2 guinea pigs -During multi-day dosing study two animals were euthanized due to adverse clinical signs.

b4

2 guinea pigs - Developed post-surgical complications, which could not be managed using pharmacological interventions. These animals were euthanized.

b4

3 dogs – 3-month oral toxicity study. All the dogs had intra-digital masses that could not be treated with analgesics because they were on study.

b4

1 dog - Found dead 48 hours after vehicle dosing.

b4

29 guinea pigs – Developed severe responses while on study and were either euthanized or found dead.

3. Justification for procedure:

b4

Pharmacokinetic Evaluation of Investigational Drugs

This protocol is used to understand how the biological system handles new chemical entities. Specifically, these are the first experiments wherein compounds from different therapeutic classes are administered via the intravascular and other routes to animals to calculate the pharmacokinetic parameters. This information is used to optimize the molecules from safety and efficacy perspective. Bioavailability is a complex process of absorption (active and passive), distribution, metabolism and elimination (ADME) and the integrated net effect requires the use of animals.

b4

Evaluation of the Electrocardiography in Anesthetized Guinea Pig

The objective of this protocol is to evaluate drug-induced changes on ECG, especially on QT interval. Antihistamines, neuroleptics and many other classes of drugs have been demonstrated to inhibit so called hERG channel in the membrane of cardiac cells. The inhibition of the hERG channel will reduce potassium transport across cell membranes and may result in QT prolongation in ECG. The QT prolongation may further induce cardiac arrhythmias (e.g. Torsade de Pointes, TdP) or cardiac arrest. The guinea pig is a good model when evaluating the hERG channel.

b4

Toxicity Studies in Rats, Mice, Dogs, Rabbits, and Guinea Pigs

The international regulatory process to approve new drug formulations and candidate drugs requires drug safety assessments. The goal of these studies is to investigate the toxicity of a new drug or formulation. The administration of any pain relieving drugs to these animals could interact and alter the results of the study.

b4

The goals of preclinical absorption, distribution, metabolism and excretion (ADME) studies are to assist in the interpretation of animal safety studies and in the design and optimization of the first administration of a new chemical entity (NCE) to humans. Typical in vivo preclinical ADME studies include animal

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pharmacokinetic (PK), mass balance, and tissue distribution studies as well as the profiling and identification of in vivo metabolites. In all, these studies describe how a mammalian system affects a NCE in terms of how fast and to what extent it is absorbed, how it is distributed into tissues, how it is metabolized, and by what route(s) it is excreted from the body.

b4

Guinea pig models for drug discovery

The guinea pig is a valuable animal model for discovery and development of treatments and potential candidate drugs.

4. Procedure required by:

b4

Agency: FDA Federal Food, Drug, and Cosmetic Act CFR: 505 (4) (i) (1) (A)